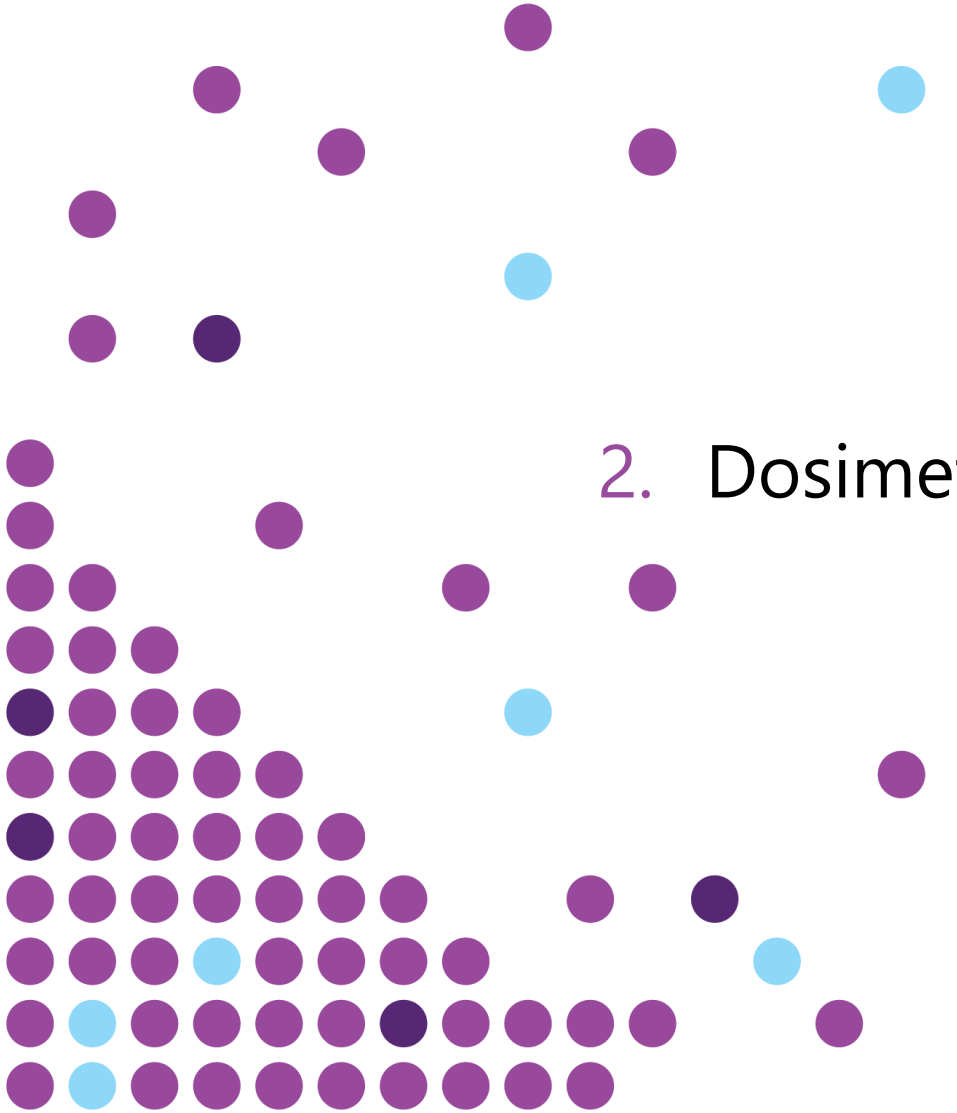
sck cen
Belgian Nuclear Research Centre

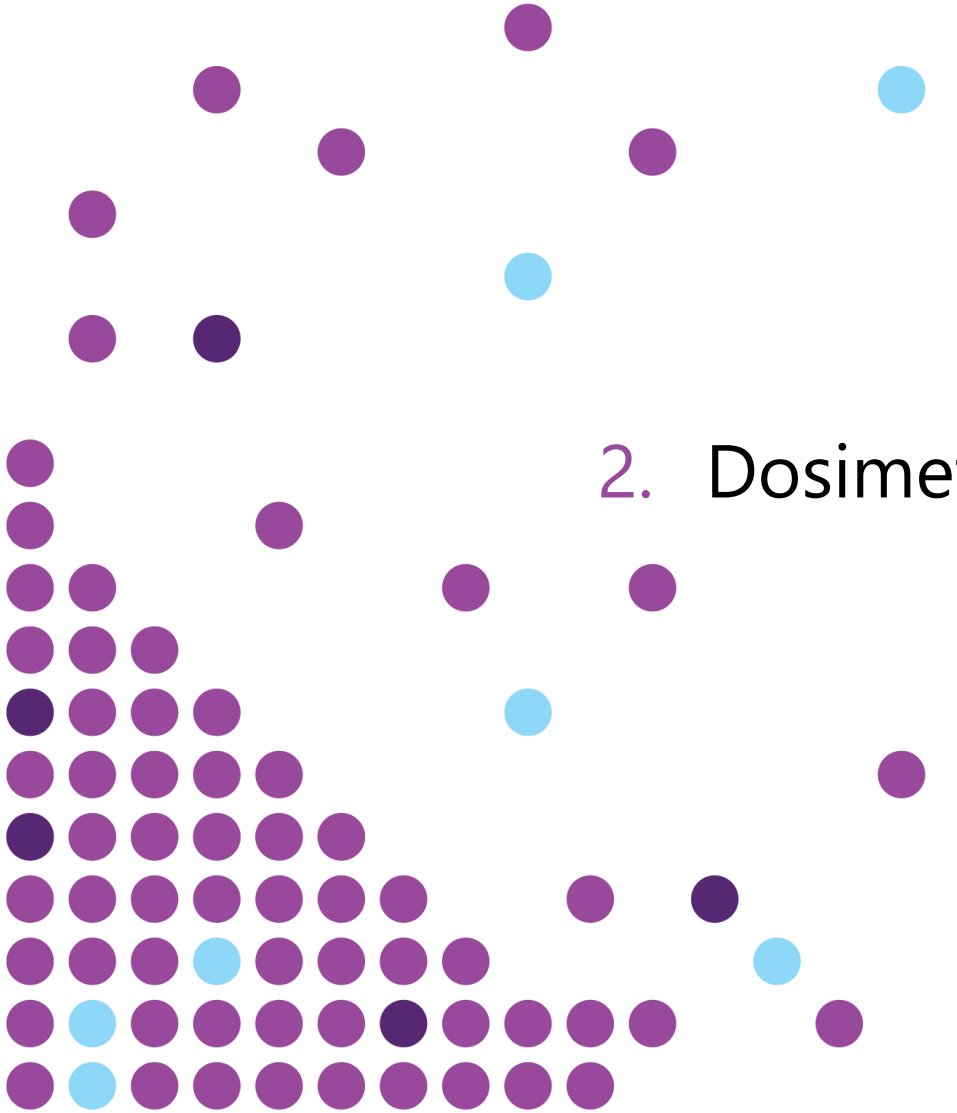
EURADOS

Radiotherapy during pregnancy

Marijke De Saint-Hubert 25/5/2023



1. Current clinical practice & data
2. Dosimetry challenges in pregnancy radiotherapy
3. EURADOS activities & plans



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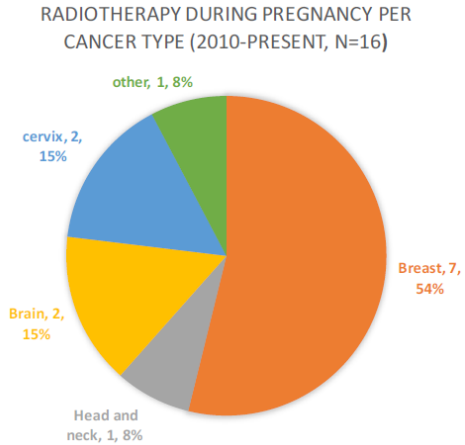
Current clinical practice

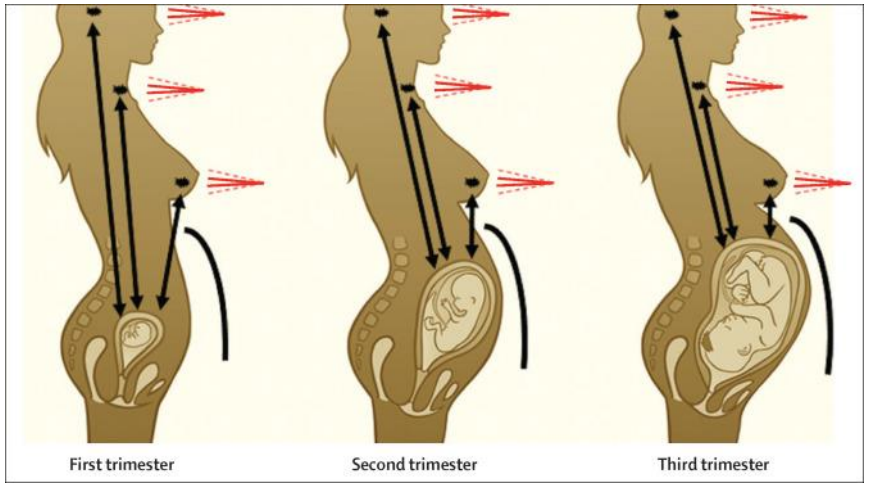
- 1 in 1000 pregnancies are complicated with cancer
- More than 70% of patients are treated during pregnancy
- Radiotherapy is only applied in less than 3% of the cases
  - Mostly breast (54%) and brain cancers (15%)
  - In first trimester can be an alternative to chemotherapy avoiding treatment delays
  - Generally radiotherapy is postponed till after delivery



- Radiotherapy during pregnancy treated as a prohibited topic
  - → Lack of reliable information on the risk of fetal damage
  - → Lack of data on the dose to the fetus during pregnancy
  - → What dose is considered allowed?
    - → ICRP - Threshold for deterministic effects (e.g. malformations) 100-200 mGy
    - → Generally a threshold of 100 mGy is used
    - → ICRP - Embryo doses of 10 mGy may increase the risk of cancer to 40% over normal incidence

General aspects of RT during pregnancy

- Fetus dose is dependent on cancer position
  - Larger the distance between tumor and fetus the better
  - Generally assumed for upper body parts RT is possible
- Fetus dose will also depend on the stage of pregnancy
  - 1st trimester is further than 2nd and 3rd trimester
  - Safe RT < 3rd trimester
- Fetal shielding is generally applied in conventional radiotherapy
  - Dose reduction factor 2-4
  - Heavy materials
    - Strong supports
      - Risks
    - Lead apron
      - Not very comfortable for patient



T Vandenbroucke, et al. The Lancet 2017. Effects of cancer treatment during pregnancy on fetal and child development

F. Amant et al. / Best Practice & Research Clinical Obstetrics and Gynaecology 29 (2015)

https://www.iaea.org/resources/rpop/health-professionals/radiology/pregnant-women

Clinical fetus dose data

Few studies on reported fetus doses and outcome

- Review paper HB Kal et al., reporting fetus dose during pregnancy photon radiotherapy
  - Breast carcinoma: fetus dose 40-180 mGy
  - Hodgkin's disease: fetus dose 9-500 mGy
  - Brain tumours: fetus dose 3-90 mGy
- For breast and Hodgkin's disease shielding was always applied while for brain, H&N only in 1 case
- Outcomes of children are reassuring, but long-term follow-up is limited

Maternal dose (Gy)	Fetal dose (Gy)	Pregnancy trimester	n	Delivery	Ref
Breast carcinoma*					
50	0·160	3	1	Healthy boy	27
50	0·14–0·18	3	1		28
46	0·039	1	1	Healthy boy	29
Hodgkin's disease*					
35–40	0·014–0·055 (6 MV) 0·100–0·136 (cobalt)	1–3	16	Healthy babies/ no malignant disease	25
19	0·09–0·42, head 0·114	3	1	Healthy child at age 8 years	33
15–20	0·020–0·50	2–3	7	Healthy children at age 6–11 years	34
			16	Healthy babies	36
35	<0·1	2	1	Healthy child	37
Brain tumours, head and neck cancer†					
64	0·027–0·086	2	1	Healthy baby	33
45	0·020	1	1		41
25	0·0015–0·0031	3	1		42
30	0·003	2	1	Healthy boy at age 3 years	43
68	0·06	3	1	Healthy girl at age 2·5 years	44
78·2	0·030	3	1	Healthy girl at age 1·5 years	44
66	0·033–0·086*	3	1		45

*With shielding. †Without shielding.

Table 2: **Total dose, fetal dose and outcome of pregnant patients undergoing radiotherapy**

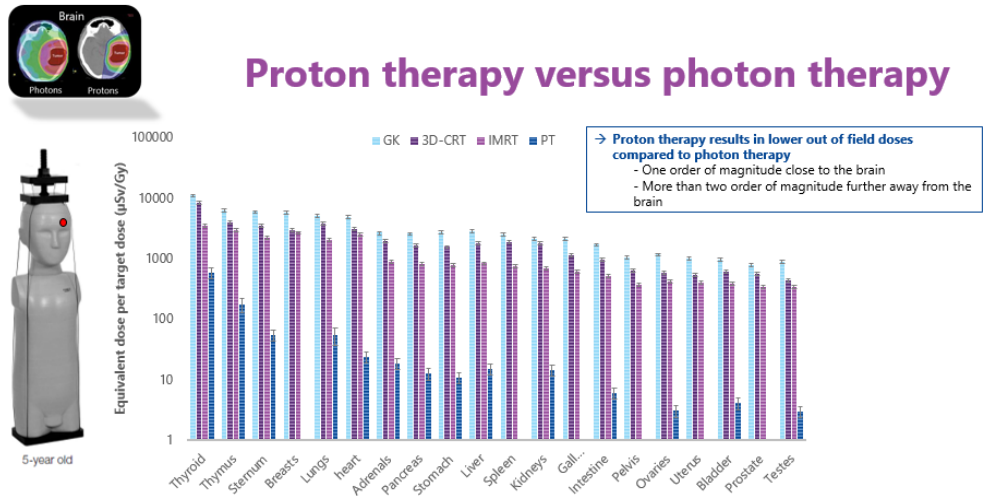
H.B. Kal and H. Struikmans, Radiotherapy during pregnancy: fact and fiction, The Lancet Oncology 6(5), 328–333 (2005).

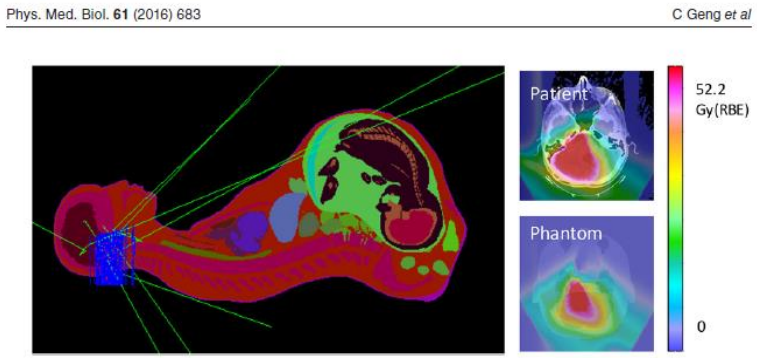
AAPM guidelines require the estimation and reduction of fetus dose
→ Protocols and guidelines to estimate fetus dose in clinical setting are still missing

Proton therapy during pregnancy

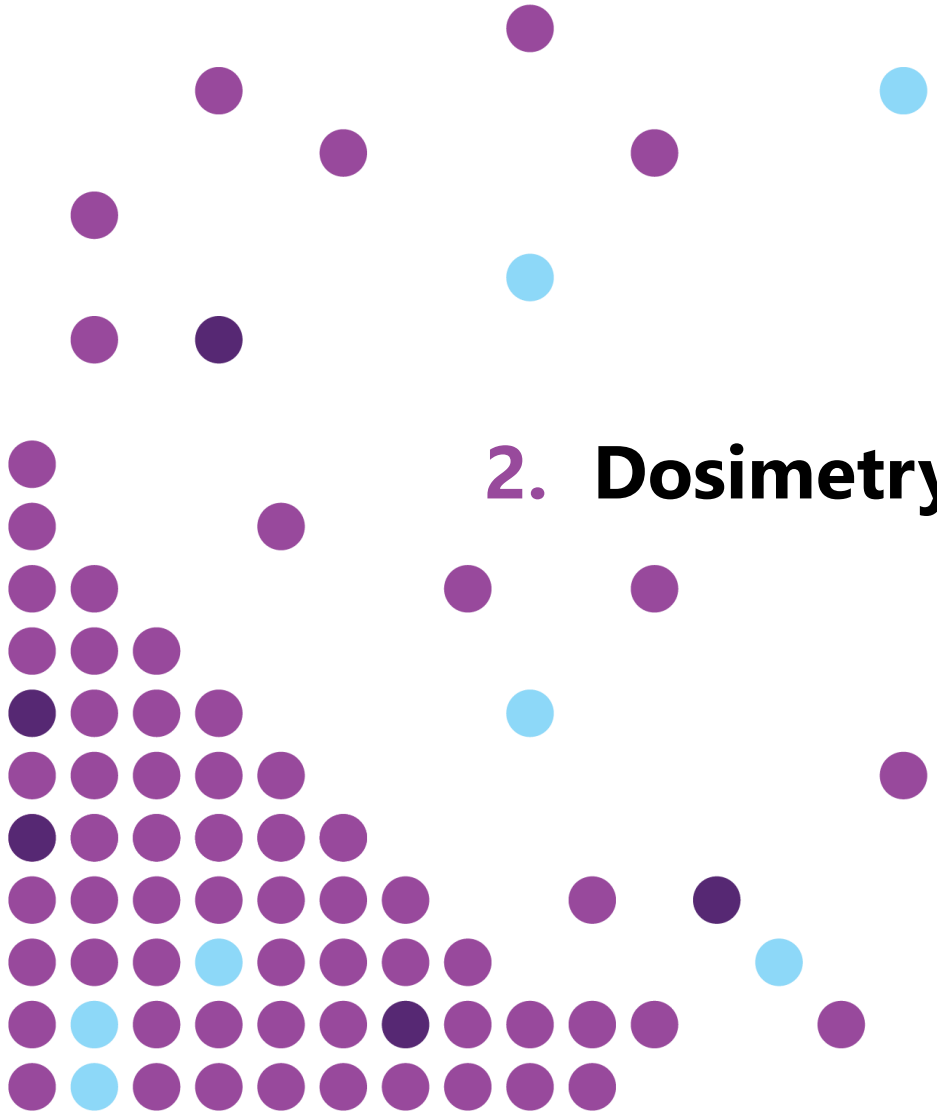
- Proton Pencil beam scanning (PBS) therapy could reduce out-of-field doses when compared to conventional radiotherapy (WG9)
- Currently only one center in Europe using proton therapy – Heidelberg
- Out-of-field doses in proton PBS therapy dominated by neutrons
  - Dosimetry challenges
  - Biological impact of neutrons
- Few studies show over a tenfold reduction in fetus dose for proton therapy compared to state-of-the-art photon therapy

Its implementation is still faced with dosimetric challenges and a lack of data and clear guidelines





Brain Pencil Beam Scanning versus 3D-CRT
- PBS (1.5-2.5 uSv/Gy)
- 3D-CRT (11-30uSv/Gy)



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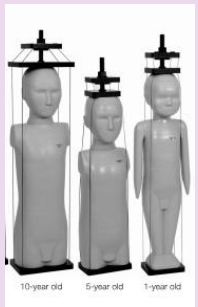
Anthropomorphic phantom of pregnant women

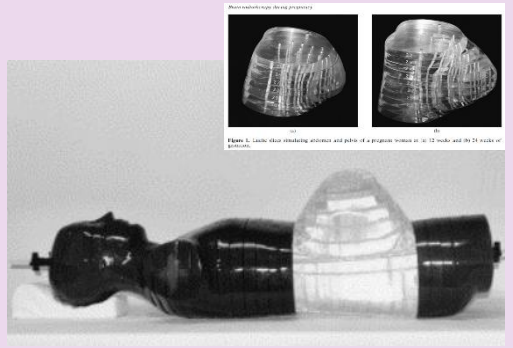
Water phantoms

Anthropomorphic

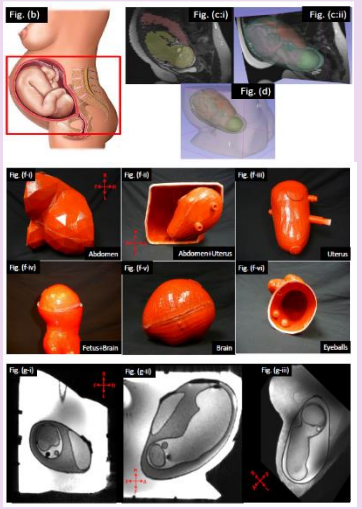


Pregnant women

- No commercial phantom exists
  - Water phantoms
    - No patient geometry and tissue composition
  - Rando phantom
    - 1st stage of pregnancy (uterus dose)
  - Rando plus PMMA/lucite slices
    - Belly of different sizes
    - Inserts for detectors
  - 3D printing technology
    - Fetus organs can be modelled



LS Chitty 1994

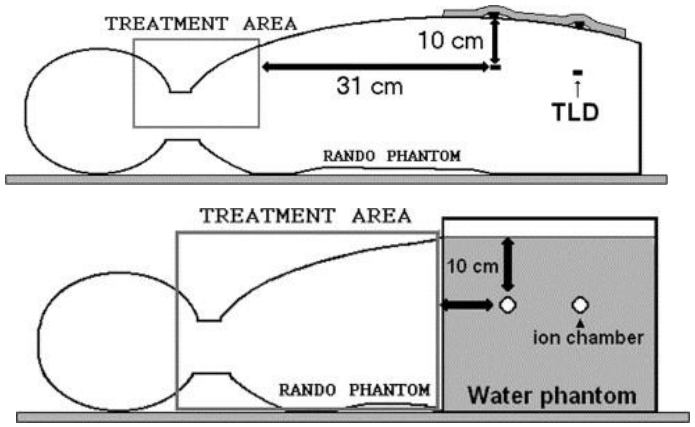


Group from USA (Boston, MA) designed and built MRI phantom that mimics critical organs (torso, uterus, placenta, fetal brain and body) and typical fetal motion in pregnancy at 36-weeks of gestational age

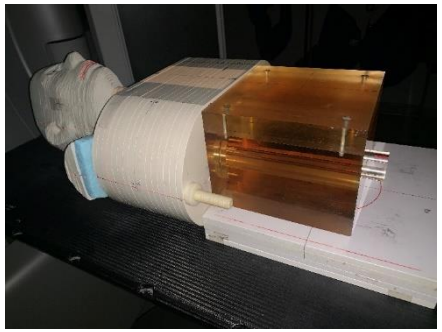
Current measurements in clinics

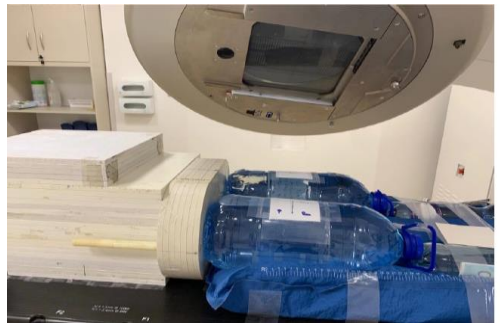
Fetal dose measurements

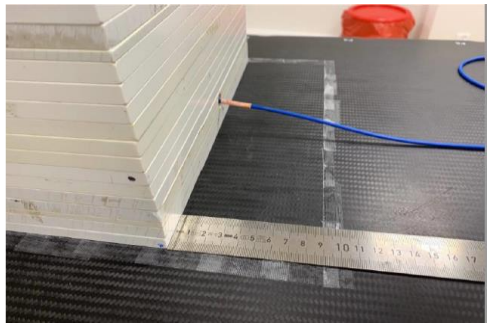
- Anthropomorphic phantom is used
  - Slabs of phantom
  - Water phantom added
- Combination of phantom pieces and water bottles
- TLDs, Ionization chambers are inserted and/or place on phantom



J.J. Nuyttens, et al. Cancer 2002







Provided by A. Kuchcińska., et al. NIO-PIB, Warsaw Poland

Z.E. Labby, et al. Rad Oncol Phys 2018

Need to develop pregnant phantoms of various stages of pregnancy

Calculations of fetal doses

- Patient imaging data are limited to the treatment area
  - Fetus is not scanned to avoid imaging dose to the fetus
- Make use of computational phantoms
  - Katja phantom – 24 weeks pregnancy (Helmholtz Zentrum Munich)
  - University of Florida family of anthropomorphic phantoms
    - 8, 10, 15, 25, 30 and 35w after conception

Figure 1. Katja and the foetus on the left hand side, on the right the primal model ICRP-AF. Clearly visible is the shifted colon. In the pelvis of ICRP-AF is the unchanged uterus

J. Becker, et al. Pol J Med Phys Eng 2008

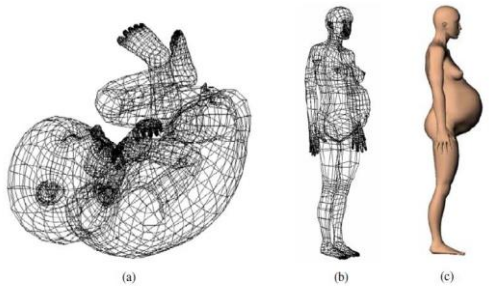
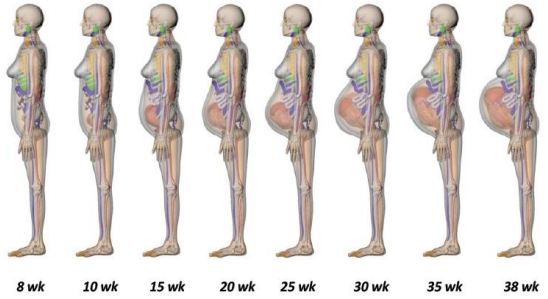
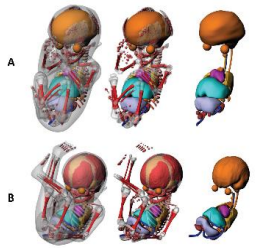


Figure 4. Models of the 9-month old fetus and the mother. (a) The adjusted skin surface model of the fetus model in mesh, (b) the adjusted skin model of the mother in mesh to accommodate for the fetus at 9-month gestation, (c) a surface rendering showing that the skin of the mother contains a 9-month old fetus.

UF/NCI Phantom Library – Pregnant Females





The UF Family of hybrid phantoms of the pregnant female for computational radiation dosimetry
Phys. Med. Biol. **59** (2014) 4325–4343
Matthew R Maynard[1], Nella S Long[1], Nash S Mowad[2], Roger Y Shifrin[1], Amy M Geyer[1], Grant Fong[1] and Wesley E Bolch[1,3]

The UF family of hybrid phantoms of the developing human fetus for computational radiation dosimetry
Phys. Med. Biol. **56** (2011) 4839–4879
Matthew R Maynard[1], John W Geyer[1], John P Aris[2], Roger Y Shifrin[1] and Wesley Bolch[1,2,3]

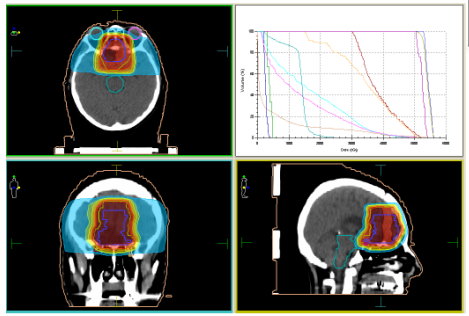
Further developments needed to allow for patient-specific dosimetry

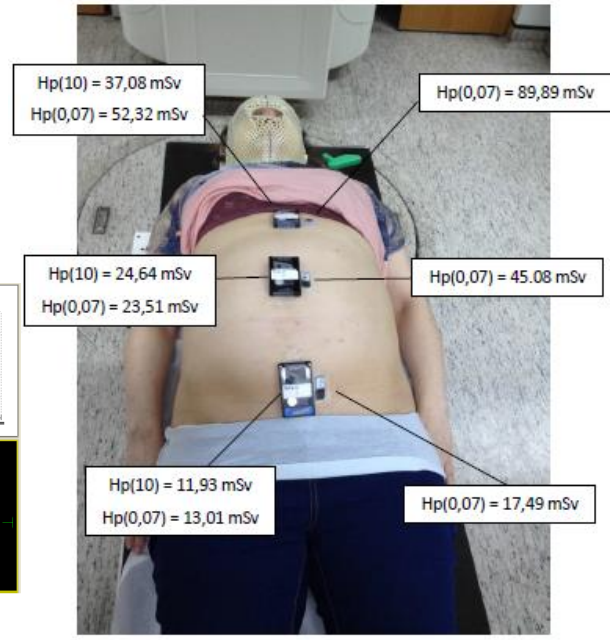
In vivo patient dosimetry in clinics

- Passive detectors on patient skin
- Assess skin dose and make use of phantom measurements for conversion to fetus dose

Sarcoma patient receiving RT during pregnancy

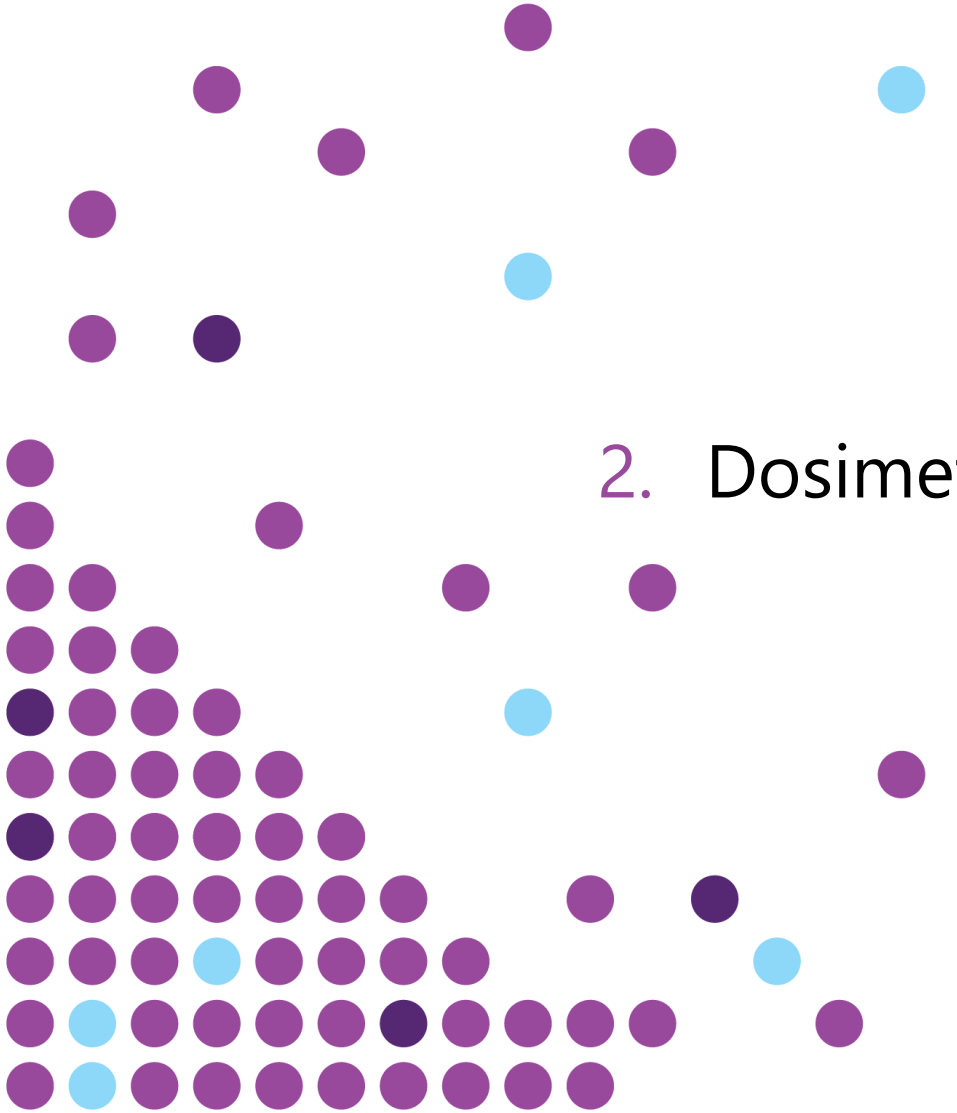
Provided by A. Kuchcińska., et al. NIO-PIB





37y old pregnant women (21 weeks pregnant) with papilar meningioma (Grade III) is treated with 3D-CRT

Develop standardized protocols for in vivo dosimetry



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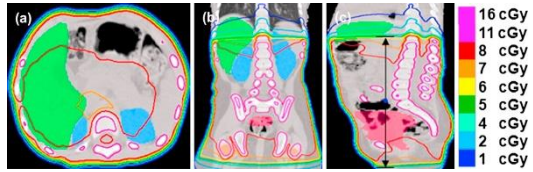
EURADOS

WG6

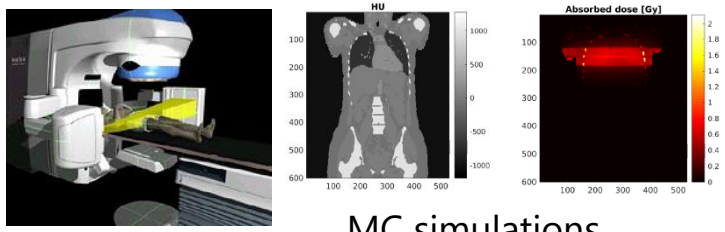
WG12

WG9

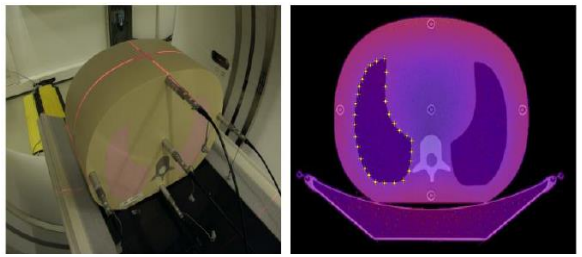
Total fetus dose including imaging dose



Imaging dose optimization

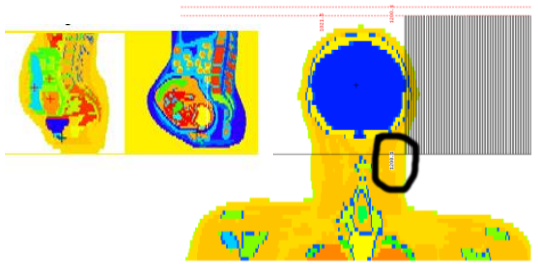


MC simulations

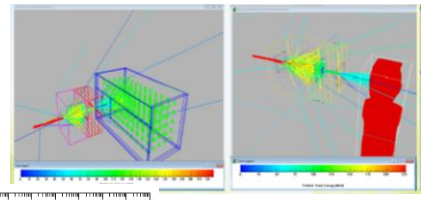


Measurements for imaging

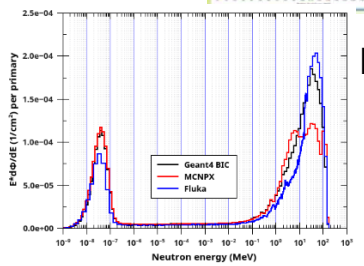
Monte Carlo simulation framework



Computational phantoms



Beam modeling

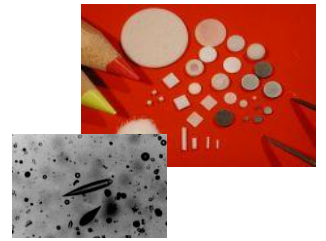


MC modeling of neutrons

Measurement campaigns in RT clinics

Phantom measurements of fetus doses in proton and photon radiotherapy

Phantom development



Detectors

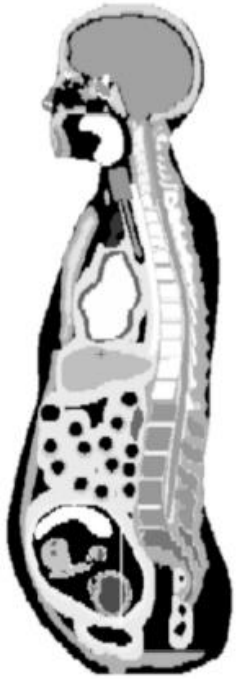
Monte Carlo simulation framework

- Computational phantoms to calculate fetus dose

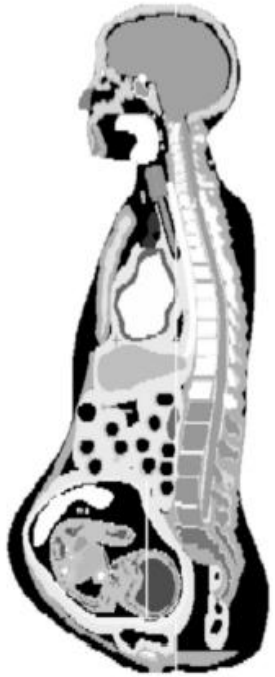
Phantom	Katja	UF20	UF25
Weeks of pregnancy	24	22	27
Female height [cm]	168	164	164
Female mass [kg]	63.6	63.6	65.8
Fetus mass [g]	730	468	986
Voxel size [mm^3]	1.775 × 1.775 × 4.84	1.26 × 1.26 × 2.7 Mother 0.301 × 0.301 × 0.301 Fetus	1.26 × 1.26 × 2.7 Mother 0.381 × 0.381 × 0.381 Fetus
Number of voxels ($*10^6$)	15.7	53.65 fetus 57.24 Mother	51.96 fetus 66.78 Mother

Katja (24 weeks)

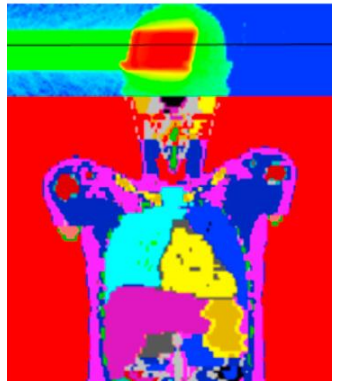
UF20 (22 weeks)



UF25 (27 weeks)



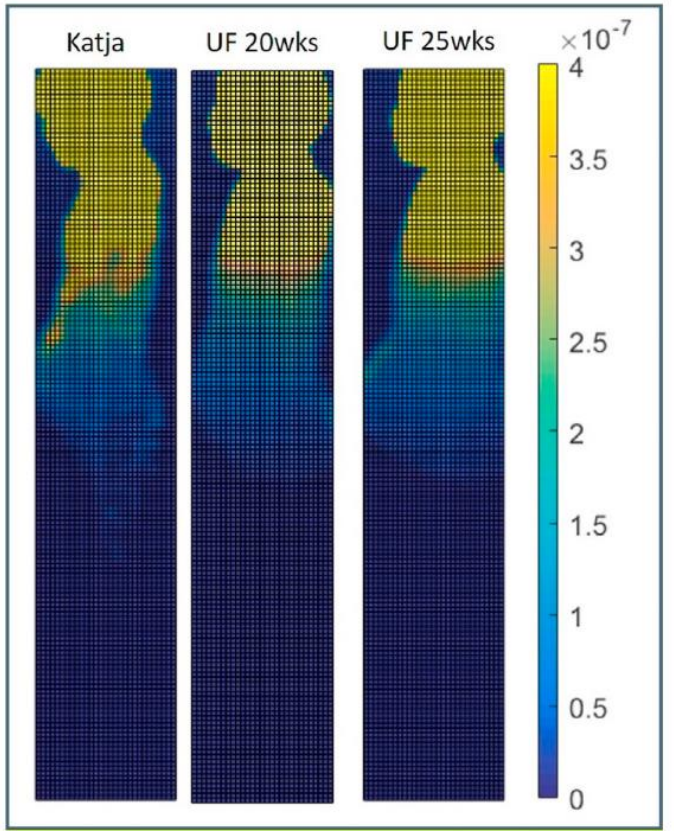
- Proton brain radiotherapy
  - 3cm collimated proton beam
  - Range 10cm and modulation 5cm



Monte Carlo simulation framework

- Highest fetus dose measured in Katja fetus
  - 780 nSv/Gy
  - ± 50 µSv (60 Gy target dose)
- UF20 and UF25 dose was 50 % lower
- No impact of different tissue compositions
- Geometrical differences
  - Katja is thinner
  - Tilted head
  - Fetus positioning is different (Katja fetus is closer)

	Dose quantities			Difference to Katja (%)	
	Katja	UF20	UF25	UF20	UF25
Photon dose per target dose [nGy/Gy]	108	60	64	44%	40%
Neutron dose equivalent per target dose [nSv/Gy]	672	295	332	56%	51%
Total dose equivalent per target dose [nSv/Gy]	780	355	396	54%	49%



Important challenges towards individualized dosimetry approaches in clinical settings

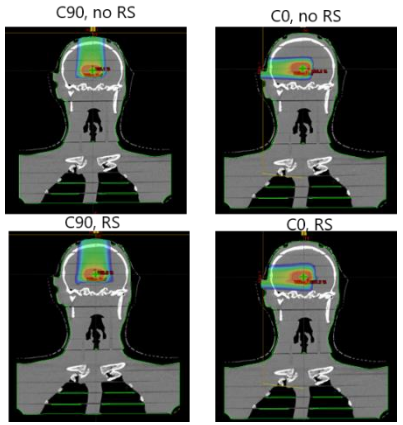
M. De Saint-Hubert, et al. Rad Meas 2021. Fetus dose calculation during proton therapy of pregnant phantoms using MCNPX and MCNP6.2 codes.

Phantom measurements for fetus doses in proton PBS therapy

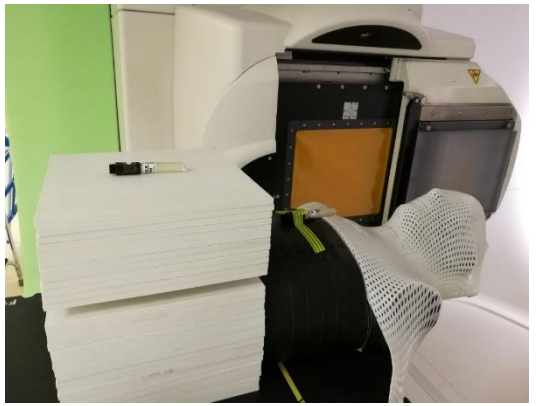
INSTYTUT FIZYKI JĄDROWEJ IM. HENRYKA NIEWODNICZAŃSKIEGO POLSKIEJ AKADEMII NAUK

Four clinical proton PBS treatment plans:

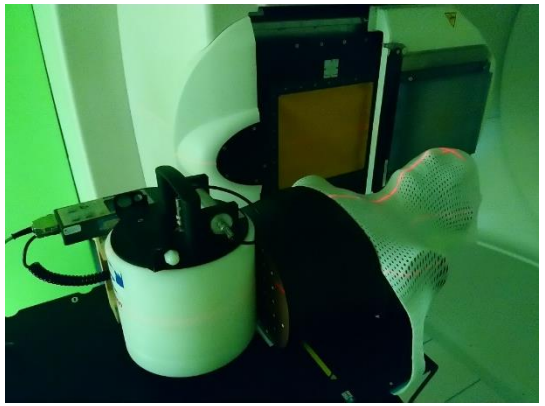
- Spherical tumor located in brain
- 2 different coach rotations (0 and 90)
- With and without range shifter
- 30fx of 2Gy



Rando Alderson phantom with RW3 slabs



BD-PNDs
Fetus position
At belly for in vivo dosimetry

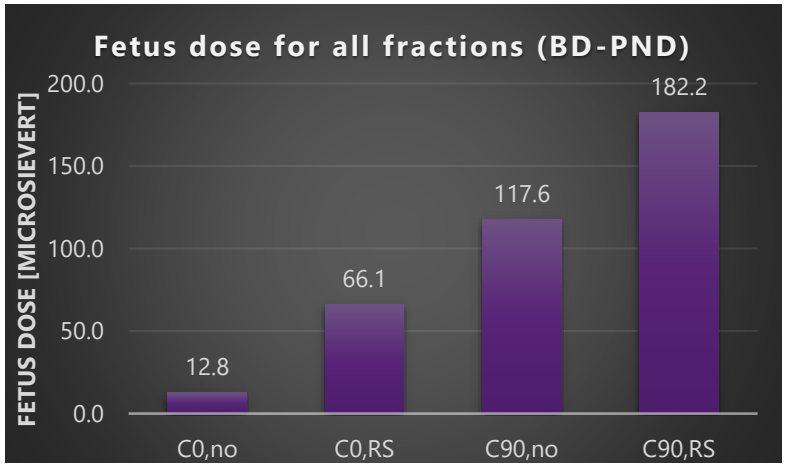


WENDI-II

Fetal doses of different plans:

- Fetus dose ranges between 13 μSv and 182 μSv
- Range shifter increased the fetal dose up to a factor of 5 (C0)
- Changing the angle from C0 to C90 increases the dose up to a factor of 9 (without RS)

- Bubble detector located at patient chest may be used for in vivo estimation of dose to the fetus delivered during each treatment session



D. Krzempek, et al. NEUDOS 2022. Measurements of neutron and gamma dose to the fetus for pregnant patients undergoing brain tumors proton radiotherapy with modulated scanning beam

Development of a pregnant female phantom

Josip Juraj Strossmayer University of Osijek Faculty of Medicine

TENA

- Second trimester (17 weeks)
  - Voxelized
  - MESH
  - DICOM
  - Physical phantom
- Phantom is subdivided in 5 cm tick slices – with inserts to hold detectors
- 3D printed molds
- 3 mixtures
  - Bones - Epoxy wax (60 %) + Si02 (5%) +CaCO3 (30 %)
  - Soft tissue – polyurethane rubber (PU) 97.2 % + 2,8% CaCO3
  - Lungs - Soft tissue mixture (92.6 %) +polystyrene (7.4 %) (2-3 mm diameter)

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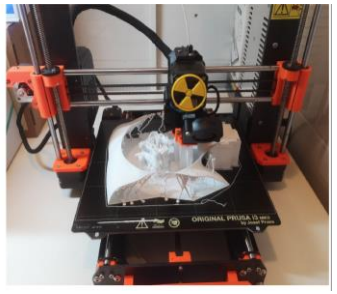
research article

Development of a computational pregnant female phantom and calculation of fetal dose during a photon breast radiotherapy

Vjekoslav Kopacin[1,2], Mladen Kasabasic[1,3], Dario Faj[1,4], Marijke de Saint Hubert[5], Stipe Galic[6], Ana Ivkovic[1,3], Marija Majer[7], Hrvoje Brkic[1,4]

[1] Department of Biophysics and Radiology, Faculty of Medicine Osijek, Osijek, Croatia
[2] Department of Diagnostic and Interventional Radiology, Osijek Clinical Hospital Centre, Osijek, Croatia
[3] Department of Medical Physics, Osijek Clinical Hospital Centre, Osijek, Croatia
[4] Department of Biophysics, Biology and Chemistry, Faculty of Dental Medicine and Health in Osijek, Osijek, Croatia
[5] Unit Research in Dosimetric Applications, Belgian Nuclear Research Centre
[6] Department of Medical Physics, University Clinical Hospital Mostar, Mostar, Bosnia and Herzegovina
[7] Division of Materials Chemistry, Ruder Bošković Institute, Zagreb, Croatia



✓ Validated in photon breast radiotherapy
→ future measurements planned in proton PBS therapy (autumn 2023)

EURADOS

Development of a belly on anthropomorphic female phantom

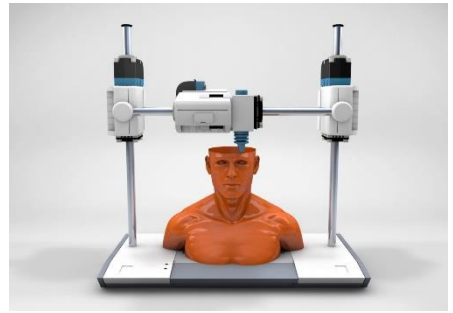
CIRS ATOM female phantom (Model number 702-D).

Developments in BfS

- 3D printer of pregnant belly on top of CIRS female phantom
- Currently testing printing approaches and materials

Developments in SCK CEN

- 2 phantom bellies on CIRS female phantom
- 10th and 30th week of pregnancy
- 3D printing in combination with lucite/PMMA



3D phantom printing

Bundesamt für Strahlenschutz

sck cen
Belgian Nuclear Research Centre

Concluding remarks

- Radiotherapy during pregnancy is not done routinely
- Proton pencil beam scanning (PBS) could reduce the dose to fetus up to more than a factor of 10
  - Clinical implementation still faces challenges due to lack of data and guidelines
- Need to develop phantoms and dosimetry protocols to perform accurate dosimetry of fetal dose
- Computational phantoms need to be extended for individualized dosimetry

Thank you for your attention